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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/981,310	12/16/97	LANDEGREN	U 1209-121P

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EXAMINER	
PORTNER, V	
ART UNIT	PAPER NUMBER
1645	24

DATE MAILED: 05/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/981,310	Landegren
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 20, 2000*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-6 and 8-10* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6 and 8-10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claims 1-6 and 8-10 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Prosecution Application

2. The request filed on October 20, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/981,310 is acceptable and a CPA has been established. An action on the CPA follows.

3. Applicant's arguments with respect to claims 1-6, 8-10 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1,3 and 4 recite a genus of kits drawn to reagents that comprise first, second and third affinity reagents for a protein, wherein claims 3 and 4 define affinity reagents to include cofactor and nucleic acid affinity reagents. The instant specification does not provide original descriptive support for a genus of kits that comprise three nucleic acid or three cofactor affinity reagents that bind to a single protein simultaneously. In view of the lack of original descriptive support for the now claimed genus of kits that comprise either three nucleic acids or cofactors that bind to proteins, the newly amended claims recite New Matter.

7. Claims 1, 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, and 4 depend from claim 1 and defines the affinity reagent to be a nucleic acid or cofactor. The analyte was defined to be a protein in claim 1. What three nucleic acids or cofactors all will bind to the same protein, at the same time, is not distinctly claimed. Clarification of the nucleic acid being claimed is requested.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Please Note: In so far as claims 3-4 recite the affinity reagent to be nucleic acids, the following rejection is being made of record.

9. Claims 1, 3, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Lindegren et al (US Pat. 4,988,617).

The claimed invention is directed to a test kit that comprises three affinity reagents and ligase. The first being specific affinity reagent being immobilized and the second and third having affinity for different determinants of the same macromolecule, wherein the affinity reagents are nucleic acids (claim 3).

Lindegren et al claim a kit that comprises first, second and third affinity reagents (see claim 20-28), together with a linking agent, wherein the linking agent is taught to be ligase (col. 2, lines 50 and claim 21).

The first immobilized affinity reagent is exemplified to be immobilized streptavidin that has affinity for biotin attached to an oligonucleotide to which biotin has been attached, wherein the complex of the first, second and third affinity reagents are detectable when the when macromolecule is in a sample.

The second affinity reagent is a first oligonucleotide that has affinity for a macromolecule.

The third affinity reagent is a second oligonucleotide that has affinity for the same macromolecule to which the first oligonucleotide has affinity, wherein the second and third affinity reagents have affinity for different determinants on said macromolecule.

The reference anticipates the now claimed kits.

10. Claims 1, 3,4 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Whiteley et al (US Pat. 5,962,223).

The claimed invention is directed to a kit that comprises first, second and third affinity reagents, wherein the affinity regent is a nucleic acid, one of the three affinity reagents is immobilized on the solid phase and the kit further comprises ligase.

Whiteley claims a kit that comprises first second and third nucleic acid affinity reagents, together with ligase. One of the three affinity nucleic acid reagents is immobilized through interaction with a capture probe on a solid support (see Whiteley, claims 1, 7, 9 and 12).

Inherently the reference anticipates the now claimed invention.

Claim Rejections - 35 U.S.C. § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

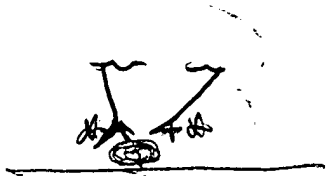
12. Claims 6, 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (US Pat. 5,635,602; filing date 1993) in view of Suzuki et al (1995).

The claimed invention is directed to a method of detecting a macromolecule in a sample using first, second and third antibodies that bind to said macromolecule, wherein detection of the macromolecule is through amplification or ligation of nucleic acid oligonucleotides attached to two of the antibodies and the first antibody is immobilized on a solid support.

Cantor et al teach a method of detecting an antigen, wherein the antigen comprises at least two different epitopes, the method comprises:

contacting a sample with solid support to immobilize the macromolecule antigen(col. 33, lines 62-64),

washing the solid support (see col. 33, line 65)



incubating the sample with two antibodies modified with conjugatable oligonucleotides (see col. 34, lines 52-53) that bind to different epitopes on said macromolecule (see col. 33, lines 50-60),

washing off excess antibodies,

adding DNA **ligase** to the sample (see col. 34, lines 22-25); and

amplifying DNA by PCR.

Cantor teaches a method and suggests the formulation of a kit that comprises two antibodies that are modified with conjugatable nucleic acid molecules, wherein the method comprises the step of immobilizing the antigen on the solid phase, but differs from the instantly claimed invention by failing to show the immobilization of the antigen on the solid phase through the use of an antibody linked to the solid phase.

Suzuki et al show the immobilization of antigen to a solid phase using an antibody linked thereto in an analogous art for the purpose of detecting an antigen in a sample that evidences a thousand fold more sensitivity than other traditional immunoassay formats.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of Cantor to include a solid phase immobilized first antibody, in view of the teachings of Suzuki because, both Cantor and Suzuki are directed to the use of immuno-polymerase chain reaction immunoassays that utilize antibodies that are modified with conjugatable oligonucleic acids, and Suzuki teaches that through sandwiching an antigen between an immobilized first antibody and an antibody that is modified with an amplifiable label,

an immunoassay with a thousand fold more sensitivity can be obtained, and Suzuki teaches that the immunoassay can be readily applied to any antigen-antibody system to which monoclonal antibodies are available.

The person of ordinary skill in the art would have been motivated by a reasonable expectation of success of detecting a macromolecule with second and third antibodies modified with amplifiable nucleic acids as taught by Cantor with an immobilized first antibody to detect a macromolecule in a sample as taught by Suzuki because Cantor et al teach macromolecules that present at least three epitopes (col. 10, lines 1-10), and the importance of detecting macromolecules that present pairs of epitopes to provide discriminating accurate analysis, where the application of an individual monoclonal antibody is insufficient for accurate analysis (see Cantor: see col. 9, lines 58 through col. 10, line 10; col. 34, lines 52-55).

13. Claims 6, 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al (US Pat. 5,635,602; filing date 1993) in view of de la Monte et al (US Pat. 5,830,670; filing date May 1995).

The claimed invention is directed to a method of detecting a macromolecule in a sample using first, second and third antibodies that bind to said macromolecule, wherein detection of the macromolecule is through amplification or ligation of nucleic acid oligonucleotides attached to two of the antibodies and the first antibody is immobilized on a solid support.

Cantor et al teach a method of detecting an antigen, wherein the antigen comprises at least two different epitopes, the method comprises:

contacting a sample with solid support to immobilize antigen(col. 33, lines 62-64),

washing the solid support (see col. 33, line 65)

incubating the sample with two antibodies modified with conjugatable oligonucleotides (see col. 34, lines 52-53) that bind to different epitopes on said macromolecule (see col. 33, lines 50-60),

washing off excess antibodies,

adding DNA **ligase** to the sample (see col. 34, lines 22-25); and

amplifying DNA by PCR .

Cantor et al teach a method and suggests the formulation of a kit that comprises two antibodies that are modified with conjugatable nucleic acid molecules, wherein the method comprises the step of immobilizing the antigen on the solid phase, but differs from the instantly claimed invention by failing to show the immobilization of the antigen on the solid phase through the use of an antibody linked to the solid phase.

de la Monte et al show a sandwich immunoassay that utilizes a plurality of antibodies directed to more than two epitopes, wherein antibodies on a solid phase immobilize the antigen and detection is accomplished through amplification of a conjugatable nucleic acid molecule attached to antibodies (see claim 6) in an analogous art for the purpose of detecting a macromolecule antigen in a sample.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of Cantor to include an immobilized first antibody, in view of the teachings of de la Monte because de la Monte teaches that through sandwiching an antigen between immobilized antibodies and antibodies specific to multiple epitopes directed to a diagnostic antigen, it is possible to diagnose the presence of a disease associated antigen through specific binding of antibodies to a plurality of epitopes (de la Monte, see claim 1).

The person of ordinary skill in the art would have been motivated by a reasonable expectation of success of detecting a macromolecule with second and third antibodies modified monoclonal antibodies with amplifiable nucleic acids as taught by Cantor with an immobilized antibody to detect a macromolecule in a sample as taught by de la Monte because Cantor et al teach macromolecules that present at least three epitopes (see Cantor, col. 10, line 7), and the importance of using an immunoassay that detects the presence of pairs of epitopes on antigens in order to provide discriminating accurate analysis where the application of an individual monoclonal antibody is insufficient for accurate analysis (see Cantor: see col. 9, lines 58 through col. 10, line 10; col. 34, lines 52-55).

14. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor in view of de la Monte.

See discussion of Cantor in view of de la Monte above.

The references teach a method of detecting a macromolecule using first, second and third antibodies, wherein two of the antibodies are modified with conjugatable nucleic acid molecules (see Cantor) together with an immobilized antibody on a solid phase that specifically binds to the same macromolecule (de la Monte), wherein ligase and PCR amplification is carried out to determine the presence or absence of an antigen in a sample. de la Monte suggests the formulation of the essential immunoassay reagents into kit form (see de la Monte, col. 25, lines 47-63) but differs from the instantly claimed invention by failing to compile all the immunoassay reagents into kit form.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to formulate immunoassay kits that comprise first, second and third antibodies, one of which is immobilized on a solid phase, and the second and third antibodies are modified with conjugatable nucleic acid molecules because de la Monte teach that immunoassay reagents are ideally suited for the preparation of a kit, wherein the kit may comprise a carrier means being compartmentalized to receive in close confinement therewith one or more container means such as vials, tubes and the like, each of said container means comprising the separate elements of the immunoassay for art recognized advantages of ease of commercialization and convenience to the user to have standardized reagents ready for carrying out the immunoassay.

15. This is a non-final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
May 7, 2001

L. F. Smith

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